Investigating Cortical Stimulation for Treating Tinnitus

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Cortical stimulation has been considered as a treatment option for several neurological disorders such as stroke, Parkinson's disease, epilepsy, and tinnitus. Our lab is currently investigating the use of auditory cortical stimulation to suppress tinnitus, which is a phantom auditory percept that is disturbing and even debilitating for millions of individuals in the U.S. alone[1]. Clinical trials utilizing invasive (via surface or penetrating electrodes) and noninvasive (via transcranial magnetic or direct current stimulation) techniques for the suppression of chronic tinnitus have produced variable results[2-6]. One concern is that the mechanism of action for cortical stimulation is still unclear, and little is known about how stimulation can affect neural firing within cortical and subcortical structures that are coding for the tinnitus. As an initial step towards understanding the effects of cortical stimulation, we systematically investigated the effect of focal electrical stimulation of the auditory cortex (AC) on the ascending auditory pathway. In particular, we assessed whether stimulation of the AC could alter acoustic-driven neural firing within the central nucleus of the inferior colliculus (CNIC). The CNIC is the main auditory processing center in the midbrain, acts a major convergence point for ascending and descending auditory pathways, and has shown profound neurophysiological changes in tinnitus animal models and patients with chronic tinnitus[1,7].

We positioned penetrating multi-site Michigan arrays into AC and the CNIC of 16 ketamine-anesthetized guinea pigs. After characterizing the acoustic-driven responses of each site to confirm its location (i.e. frequency region and sub-nuclei of AC and CNIC), we electrically stimulated AC and recorded the corresponding changes in acoustic-driven responses throughout the CNIC. Acoustic-driven responses were recorded again after electrical stimulation had ceased to assess any residual changes.

Stimulation of AC induced widespread suppression of acoustic-driven activity throughout the CNIC. The amount of suppression varied drastically depending on the cortical region being stimulated. For example, stimulation of the medial portion of primary auditory cortex induced suppression of over half of all sites in the CNIC, while stimulation of the ventrorostral belt elicited minimal suppression. The suppression was widespread throughout the CNIC without any apparent topographic organization across the tonotopic axis nor along the isofrequency laminae. Furthermore, suppression of neural firing largely continued even after the electrical stimulation had ended. On the other hand, minimal excitation was elicited throughout the CNIC. These results indicate that cortical stimulation can have a profound and lasting suppressive effect on subcortical processing. Considering that tinnitus has been linked to hyperactivity within the central auditory system, these suppressive effects are encouraging for the use of cortical stimulation for treating tinnitus and warrants further investigation in animals and humans for improving cortical devices currently used for tinnitus treatment.

[1] C.A. Bauer, J.G. Turner, D.M. Caspary, K.S. Myers, and T.J. Brozoski. "Tinnitus and the Inferior Colliculus Activity in Chinchillas Related to Three Distinct Patterns of Cochlear Trauma." *Neuroscience Research,* vol. 86, pp. 2564-2578, April 2008.

[2] J. Song, S. Vanneste, P. Van de Heyning, and D. De Ridder. "Transcranial Current Stimulation in Tinnitus Patients: A Systemic Review and Meta-Analysis." *The Scientific World Journal,* September 2012.

[3] S. Vanneste and D. De Ridder. "Noninvasive and Invasive Neuromodulation for the Treatment of Tinnitus: An Overview." *Neuromodulation: Technology at the Neural Interface,* vol. 15, pp. 350-360, August 2012.

[4] D.R. Friedland, W. Gaggl, C. Runge-Samuelson, J.L. Ulmer, and B.H. Kopell. "Feasibility of Auditory Cortical Stimulation for the Treatment of Tinnitus." *Otology & Neurotology,* vol. 28, pp. 1005-1012, December 2007.

[5] M.D. Seidman, D. De Ridder, K. Elisevich, S.M. Bowyer, I. Darrat, J. Dria, B. Stach, Q. Jiang, N. Tepley, J. Ewing, M. Seidman, and J. Zhang. "Direct Electrical Stimulation of Heschl's Gyrus for Tinnitus Treatment." *The Laryngoscope,* vol. 118, pp. 491-500, March 2008.

[6] S.M. Theodoroff and R.L. Folmer. "Repetitive Transcranial Magnetic Stimulation as a Treatment for Chronic Tinnitus: A Critical Review." *Otology & Neurotology,* vol. 34, pp. 199-208, February 2013.

[7] C.P. Lanting, E. de Kleine, and P. van Dijk. "Neural activity underlying tinnitus generation: Results from PET and fMRI." *Hearing Research,* vol. 255, pp. 1-13, June 2009.

This work was supported by NIH NIDA award number T32DA022616, NIH NIDCD award number R03-DC011589, the University of Minnesota Frieda Martha Kunze Fellowship, the University of Minnesota Institute for Engineering in Medicine Walter Barnes Lange Memorial Award, and start-up funds from the University of Minnesota (Institute for Translational Neuroscience and College of Science and Engineering).

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